REPORT ON MONITORING OF ADVERSE DRUG REACTIONS DUE TO ANTIMALARIAL USE IN TANZANIA

2006 - 2008
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADRs</td>
<td>Adverse Drug Reactions</td>
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<tr>
<td>ALu</td>
<td>Artemether + Lumefantrine</td>
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<td>BMC</td>
<td>Bugando Medical Centre</td>
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<td>CEM</td>
<td>Cohort Event Monitoring</td>
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<td>GF</td>
<td>Global Funds</td>
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<td>KCMC</td>
<td>Kilimanjaro Christian Medical Centre</td>
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<td>MNH</td>
<td>Muhimbili National Hospital</td>
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<td>TFDA</td>
<td>Tanzania Food and Drugs Authority</td>
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<td>UMC</td>
<td>Uppsala Monitoring Centre</td>
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<td>WHO</td>
<td>World Health Organization</td>
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1. Introduction

Tanzania Food and Drugs Authority (TFDA) is the Regulatory Authority which had been established by the Act of Parliament - the Tanzania Food, Drugs and Cosmetics Act, 2003. Amongst other functions, the Authority has been mandated to monitor safety of medicines consumed by Tanzanians. It is required to ensure that existing and new adverse events, interactions and information about pharmacovigilance of products are being monitored globally, analyzed and acted upon.

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. The principal aims of pharmacovigilance include:

- To improve patient care and safety in relation to the use of medicines, and all medical and paramedical interventions;
- To improve public health and safety in relation to the use of medicines;
- To detect problems related to the use of medicines and communicate the findings in a timely manner;
- To contribute to the assessment of benefit, harm, effectiveness and risk of medicines leading to the prevention of harm and maximization of benefit,
- To encourage the safe, rational and more effective (including cost-effective) use of medicines;
- To promote understanding, education and clinical training in pharmacovigilance and its effective communication to health professionals and the public.

2. Pharmacovigilance System

Pharmacovigilance activities in Tanzania started way back in 1989. TFDA joined the World Health Organization (WHO) Programme for International Drug Monitoring in 1993. Since then the Authority has been sharing information with other Member States through database (also known as Vigiflow) developed by WHO at its Uppsala Monitoring Centre (UMC) in Sweden.

The system is coordinated by TFDA through its headquarter offices in Dar-es-Salaam as well as established pharmacovigilance centers located at Muhimbili National Hospital (MNH) - Dar-es-Salaam, Bugando Medical Centre (BMC) - Mwanza, Kilimanjaro Christian Medical Centre (KCMC) - Moshi and Mbeya Regional Hospital - Mbeya.
The system uses printed forms (Yellow Forms) which have been designed to collect data from reporters. Upon receiving ADR reports, data are usually assessed for causality and then entered into the Vigiflow.

3. Monitoring of ADRs due to Antimalarial use

The Authority has been receiving funds from the Global Fund to fight Malaria, HIV/AIDS and TB (GF) to strengthen its pharmacovigilance system. The funds among other things have enabled TFDA to sensitize healthcare providers to report ADRs, develop various ADR Guidelines and convene Expert Committee meetings to deliberate on pharmacovigilance issues and therefore simplify the decision-making process. Apart from monitoring antiretroviral and antituberculous agents, the funds have also been used to monitor the safety of antimalarials in the country.

As the system is passive in the sense that reporters decide to report on their own discretion (voluntarily), few ADR reports due to antimalarial use were received over the past two years (2006 – 2008). A summary of the reports received is appended as Annex 1 to this report which also includes reports for each individual case as recorded in the Vigiflow.

Mainly, two medicines (i.e. Artemether + Lumefantrine – ALu and Sulpha containing antimalarial agents – SP) have been implicated to the observed ADRs. A total of 18 cases were reported which included 12 for ALu (Coartem), 2 for Metakelfin, 1 for Laefin and 3 for Sulfadoxine + Pyrimethamine (Fansidar).

Majority of reports originated from where pharmacovigilance centres are located (i.e. Mwanza, Moshi and Mbeya). Other reports came from few hospitals/ dispensaries in Morogoro, Shinyanga and Rufiji. Reporters were mostly physicians, pharmacists and other health professionals (i.e. not physicians or pharmacists). Most of the reports were non serious. Serious reports are those which:

- Results into death
- Are life threatening (i.e. where the patient was at risk of death at the time of the reaction, not a reaction which hypothetically might have been fatal if it were more severe)
- Requires inpatient hospitalization or prolongation of existing one
- Results into persistent or significant disability/ incapacity
- Results into congenital anomaly/ birth defect
- Others - drug interaction reports (except well known) and medically important reactions e.g. hepatic, renal or haematological.
Assessment which was done on ADR reports shows that many were probably or possibly related to the drug used. A total of 10 possible and 8 probable relationships were observed. Annex 2 of this report describes the causality rating used by TFDA when assessing ADR reports.

4. Conclusion

It is certain that few reports were received in the last two years and more work needs to be done to sensitize healthcare professionals and the general public to increase ADR reporting rate.

As a result of these few reports, no concrete regulatory decisions have been taken which could have otherwise lead to change of product labels, introducing new warnings or precautions on product information leaflets or complete removal of a product from the market.

5. Future Plans

Due to low reporting rate which has been a chronic hindrance to successful and effective pharmacovigilance system and largely attributed to the passive or spontaneous reporting mechanism, TFDA is now planning to adopt an active surveillance system of monitoring ADRs. This approach is scientifically termed as Cohort Event Monitoring (CEM).

CEM is a prospective, observational study of adverse events that occur during the use of a particular medicine in the early post-marketing phase. It ensures that patients are monitored from the time they begin treatment and involves patients in watching, feeling and monitoring their treatments. Advantages of CEM compared to spontaneous reporting include;

i. Active measures are taken to find adverse events.
ii. Events are proactively followed-up by asking patients directly or screening patient records.
iii. Reporting rates are high with minimal biases.
iv. Can characterize reactions in terms of age, sex and duration to onset and thus produce risk factors. Other relevant data may be collected such as weight, or co-morbidity in order to provide the opportunity for determining other risk factors.
v. Can establish a pregnancy register and define and measure rates of any abnormalities.
vi. Because of routine follow-up, can detect with confidence reduced or failed therapeutic effect and thus raise suspicion of inaccurate
diagnosis of disease, poor prescribing, inadequate adherence to treatment, emerging resistance, poor quality or counterfeit medicines.

vii. Very effective in identifying signals at an early stage.

viii. Can make accurate comparisons between medicines.

ix. Can record and examine details of all deaths and provide rates of death.

x. Can produce rapid results in a defined population.

To begin with, CEM of ALu and ARVs will be conducted in the coming two years and upon successful completion, other medicines will be subjected into surveillance. It is envisaged that the approach will also boost passive reporting in the long run.

Apart from CEM, other plans include;

i. Developing TV adverts on pharmacovigilance and air them out to the public to raise awareness.

ii. Printing and distributing adequate “Yellow Forms” to health facilities to assist in data collection.

iii. Developing “ADR Bulletin” to facilitate dissemination of information to stakeholders on ADR cases reported, analyses done and regulatory actions taken.

iv. Conducting supportive supervision of pharmacovigilance centres to monitor and evaluate performance.